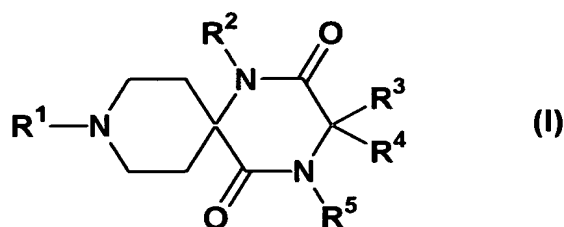


CLAIMS

1. A function inhibitor of an effector cell, which comprises a CCR5 antagonist.
2. The function inhibitor of an effector cell according to claim 1, wherein the function is cell migration, cell proliferation or cell activation.
3. The function inhibitor of an effector cell according to claim 1, wherein the effector cell is a CCR5-positive effector cell.
4. The function inhibitor of an effector cell according to claim 1, which is an agent for prevention and/or treatment of a disease caused by effector cell function.
5. The function inhibitor of an effector cell according to claim 1, which is an agent for prevention and/or treatment of a T cell-mediated disease.
6. The function inhibitor of an effector cell according to claim 1, which is an agent for prevention and/or treatment of a myeloid cell-mediated disease.
7. The function inhibitor of an effector cell according to claim 5, wherein the T cell-mediated disease is transplant rejection, autoimmune disease, allergic disease or ischemic disease.
8. The function inhibitor of an effector cell according to claim 6, wherein the myeloid cell-mediated disease is cancer or cancer metastasis.

9. The function inhibitor of an effector cell according to claim 1, wherein the CCR5 antagonist is a non-peptide substance.

10. The function inhibitor of an effector cell according to claim 1, wherein the CCR5 antagonist is a compound of formula (I)



wherein R^1 represents (1) a hydrogen atom, (2) C1-18 alkyl, (3) C2-18 alkenyl, (4) C2-18 alkynyl, (5) $-\text{COR}^6$, (6) $-\text{CONR}^7\text{R}^8$, (7) $-\text{COOR}^9$, (8) $-\text{SO}_2\text{R}^{10}$, (9) $-\text{COCOOR}^{11}$, (10) $-\text{CONR}^{12}\text{COR}^{13}$, (11) Cyc1 or (12) C1-18 alkyl, C2-18 alkenyl or C2-18 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) $-\text{CONR}^7\text{R}^8$, (c) $-\text{COOR}^9$, (d) $-\text{OR}^{14}$, (e) $-\text{SR}^{15}$, (f) $-\text{NR}^{16}\text{R}^{17}$, (g) $-\text{NR}^{18}\text{COR}^{19}$, (h) $-\text{SO}_2\text{NR}^{20}\text{R}^{21}$, (i) $-\text{OCOR}^{22}$, (j) $-\text{NR}^{23}\text{SO}_2\text{R}^{24}$, (k) $-\text{NR}^{25}\text{COOR}^{26}$, (l) $-\text{NR}^{27}\text{CONR}^{28}\text{R}^{29}$, (m) Cyc1, (n) keto and (o) $-\text{N}(\text{SO}_2\text{R}^{24})_2$;

$\text{R}^6\text{-R}^9$, $\text{R}^{11}\text{-R}^{21}$, R^{23} , R^{25} and $\text{R}^{27}\text{-R}^{29}$ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc1 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) Cyc1, (b) halogen, (c) $-\text{OR}^{30}$, (d) $-\text{SR}^{31}$, (e) $-\text{NR}^{32}\text{R}^{33}$, (f) $-\text{COOR}^{34}$, (g) $-\text{CONR}^{35}\text{R}^{36}$, (h) $-\text{NR}^{37}\text{COR}^{38}$, (i) $-\text{NR}^{39}\text{SO}_2\text{R}^{40}$ and (j) $-\text{N}(\text{SO}_2\text{R}^{40})_2$, or

R^7 and R^8 , R^{20} and R^{21} , or R^{28} and R^{29} are taken together to represent (1) C2-6 alkylene, (2) $-(\text{C2-6 alkylene})\text{-O-}(\text{C2-6 alkylene})\text{-}$, (3) $-(\text{C2-6 alkylene})\text{-S-}(\text{C2-6 alkylene})\text{-}$ or (4) $-(\text{C2-6 alkylene})\text{-NR}^{195}\text{-(C2-6 alkylene)-}$, wherein R^{195} is a hydrogen atom, C1-8 alkyl, phenyl, or C1-8 alkyl substituted with phenyl;

R^{10} , R^{22} , R^{24} and R^{26} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc1 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) Cyc1, (b) halogen, (c) $-OR^{30}$, (d) $-SR^{31}$, (e) $-NR^{32}R^{33}$, (f) $-COOR^{34}$, (g) $-CONR^{35}R^{36}$, (h) $-NR^{37}COR^{38}$, (i) $-NR^{39}SO_2R^{40}$ and (j) $-N(SO_2R^{40})_2$;

$R^{30}-R^{37}$ and R^{39} each independently represents a hydrogen atom, C1-8 alkyl, Cyc1 or C1-8 alkyl substituted with Cyc1, or

R^{35} and R^{36} are taken together to represent (1) C2-6 alkylene, (2) $-(C2-6 \text{ alkylene})-O-(C2-6 \text{ alkylene})-$, (3) $-(C2-6 \text{ alkylene})-S-(C2-6 \text{ alkylene})-$ or (4) $-(C2-6 \text{ alkylene})-NR^{196}-(C2-6 \text{ alkylene})-$, wherein R^{196} represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R^{38} and R^{40} each independently represents C1-8 alkyl, Cyc1 or C1-8 alkyl substituted with Cyc1;

Cyc1 represents a C3-15 mono-, bi- or tri-(fused or spiro)carbocyclic ring or a 3-15 membered mono-, bi- or tri-(fused or spiro)cyclic hetero ring containing 1-4 nitrogen atom(s), 1-3 oxygen atom(s) and/or 1-3 sulfur atom(s), and Cyc1 may be substituted with 1-5 of R^{51} ;

R^{51} represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) nitro, (6) trifluoromethyl, (7) trifluoromethoxy, (8) nitrile, (9) keto, (10) Cyc2, (11) $-OR^{52}$, (12) $-SR^{53}$, (13) $-NR^{54}R^{55}$, (14) $-COOR^{56}$, (15) $-CONR^{57}R^{58}$, (16) $-NR^{59}COR^{60}$, (17) $-SO_2NR^{61}R^{62}$, (18) $-OCOR^{63}$, (19) $-NR^{64}SO_2R^{65}$, (20) $-NR^{66}COOR^{67}$, (21) $-NR^{68}CONR^{69}R^{70}$, (22) $-B(OR^{71})_2$, (23) $-SO_2R^{72}$, (24) $-N(SO_2R^{72})_2$, or (25) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) Cyc2, (c) $-OR^{52}$, (d) $-SR^{53}$, (e) $-NR^{54}R^{55}$, (f) $-COOR^{56}$, (g) $-CONR^{57}R^{58}$, (h) $-NR^{59}COR^{60}$, (i) $-SO_2NR^{61}R^{62}$, (j) $-OCOR^{63}$,

(k) $-\text{NR}^{64}\text{SO}_2\text{R}^{65}$, (l) $-\text{NR}^{66}\text{COOR}^{67}$, (m) $-\text{NR}^{68}\text{CONR}^{69}\text{R}^{70}$, (n) $-\text{B}(\text{OR}^{71})_2$, (o) $-\text{SO}_2\text{R}^{72}$ and (p) $-\text{N}(\text{SO}_2\text{R}^{72})_2$;

$\text{R}^{52}-\text{R}^{62}$, R^{64} , R^{66} and $\text{R}^{68}-\text{R}^{71}$ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc2 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc2, $-\text{OR}^{73}$, $-\text{COOR}^{74}$ or $-\text{NR}^{75}\text{R}^{76}$, or

R^{57} and R^{58} , R^{61} and R^{62} , or R^{69} and R^{70} are taken together to represent (1) C2-6 alkylene, (2) $-(\text{C2-6 alkylene})-\text{O}-(\text{C2-6 alkylene})-$, (3) $-(\text{C2-6 alkylene})-\text{S}-(\text{C2-6 alkylene})-$ or (4) $-(\text{C2-6 alkylene})-\text{NR}^{197}-(\text{C2-6 alkylene})-$, wherein R^{197} represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R^{63} , R^{65} , R^{67} and R^{72} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc2 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc2, $-\text{OR}^{73}$, $-\text{COOR}^{74}$ or $-\text{NR}^{75}\text{R}^{76}$;

$\text{R}^{73}-\text{R}^{76}$ each independently represents a hydrogen atom, C1-8 alkyl, Cyc2 or C1-8 alkyl substituted with Cyc2;

Cyc2 has the same meaning as Cyc1, and Cyc2 may be substituted with 1-5 of R^{77} ;

R^{77} represents (1) C1-8 alkyl, (2) halogen, (3) nitro, (4) trifluoromethyl, (5) trifluoromethoxy, (6) nitrile, (7) $-\text{OR}^{78}$, (8) $-\text{NR}^{79}\text{R}^{80}$, (9) $-\text{COOR}^{81}$, (10) $-\text{SR}^{82}$, (11) $-\text{CONR}^{83}\text{R}^{84}$, (12) C2-8 alkenyl, (13) C2-8 alkynyl, (14) keto, (15) Cyc6, (16) $-\text{NR}^{161}\text{COR}^{162}$, (17) $-\text{SO}_2\text{NR}^{163}\text{R}^{164}$, (18) $-\text{OCOR}^{165}$, (19) $-\text{NR}^{166}\text{SO}_2\text{R}^{167}$, (20) $-\text{NR}^{168}\text{COOR}^{169}$, (21) $-\text{NR}^{170}\text{CONR}^{171}\text{R}^{172}$, (22) $-\text{SO}_2\text{R}^{173}$, (23) $-\text{N}(\text{SO}_2\text{R}^{167})_2$ or (24) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) $-\text{OR}^{78}$, (c) $-\text{NR}^{79}\text{R}^{80}$, (d) $-\text{COOR}^{81}$, (e) $-\text{SR}^{82}$, (f) $-\text{CONR}^{83}\text{R}^{84}$, (g) keto, (h) Cyc6, (i) $-\text{NR}^{161}\text{COR}^{162}$, (j) $-\text{SO}_2\text{NR}^{163}\text{R}^{164}$, (k) $-\text{OCOR}^{165}$, (l) $-\text{NR}^{166}\text{SO}_2\text{R}^{167}$, (m) $-\text{NR}^{168}\text{COOR}^{169}$, (n) $-\text{NR}^{170}\text{CONR}^{171}\text{R}^{172}$, (o) $-\text{SO}_2\text{R}^{173}$, and (p) $-\text{N}(\text{SO}_2\text{R}^{167})_2$;

$R^{78}-R^{84}$, $R^{161}-R^{164}$, R^{166} , R^{168} and $R^{170}-R^{172}$ each independently represents (a) a hydrogen atom, (b) C1-8 alkyl, (c) C2-8 alkenyl, (d) C2-8 alkynyl, (e) Cyc6, (f) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc6, $-OR^{174}$, $-COOR^{175}$, $-NR^{176}R^{177}$ or $-CONR^{178}R^{179}$, or

R^{83} and R^{84} , R^{163} and R^{164} , or R^{171} and R^{172} are taken together to represent (1) C2-6 alkylene, (2) $-(C2-6 \text{ alkylene})-O-(C2-6 \text{ alkylene})-$, (3) $-(C2-6 \text{ alkylene})-S-(C2-6 \text{ alkylene})-$ or (4) $-(C2-6 \text{ alkylene})-NR^{198}-(C2-6 \text{ alkylene})-$, wherein R^{198} represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R^{165} , R^{167} , R^{169} and R^{173} each independently represents (a) C1-8 alkyl, (b) C2-8 alkenyl, (c) C2-8 alkynyl, (d) Cyc6 or (e) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc6, $-OR^{174}$, $-COOR^{175}$, $-NR^{176}R^{177}$ or $-CONR^{178}R^{179}$;

$R^{174}-R^{177}$ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) Cyc6 or (4) C1-8 alkyl substituted with Cyc6, or

R^{178} and R^{179} are taken together to represent (1) C2-6 alkylene, (2) $-(C2-6 \text{ alkylene})-O-(C2-6 \text{ alkylene})-$, (3) $-(C2-6 \text{ alkylene})-S-(C2-6 \text{ alkylene})-$ or (4) $-(C2-6 \text{ alkylene})-NR^{199}-(C2-6 \text{ alkylene})-$, wherein R^{199} represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

Cyc6 represents a C3-8 mono-carbocyclic ring or a 3-8 membered monocyclic hetero ring containing 1-4 nitrogen atom(s), 1-2 oxygen atom(s) and/or 1-2 sulfur atom(s), with the proviso that, Cyc6 may be substituted with 1-5 of R^{180} ;

R^{180} represents (1) C1-8 alkyl, (2) halogen, (3) nitro, (4) trifluoromethyl, (5) trifluoromethoxy, (6) nitrile, (7) $-OR^{181}$, (8) $-NR^{182}R^{183}$, (9) $-COOR^{184}$, (10) $-SR^{185}$ or (11) $-CONR^{186}R^{187}$;

$R^{181}-R^{187}$ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) phenyl or (4) C1-8 alkyl substituted with phenyl, or

R^{182} and R^{183} , or R^{186} and R^{187} are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)- NR^{200} -(C2-6 alkylene)-, wherein R^{200} represents a hydrogen atom, C1-8 alkyl, phenyl, C1-8 alkyl substituted with phenyl;

R^2 represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) - OR^{90} , (6) Cyc3 or (7) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) - OR^{90} , (c) - SR^{91} , (d) - $NR^{92}R^{93}$, (e) - $COOR^{94}$, (f) - $CONR^{95}R^{96}$, (g) - $NR^{97}COR^{98}$, (h) - $SO_2NR^{99}R^{100}$, (i) - $OCOR^{101}$, (j) - $NR^{102}SO_2R^{103}$, (k) - $NR^{104}COOR^{105}$, (l) - $NR^{106}CONR^{107}R^{108}$, (m) Cyc3, (n) keto and (o) - $N(SO_2R^{103})_2$;

R^{90} - R^{100} , R^{102} , R^{104} and R^{106} - R^{108} each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc3 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc3, or

R^{95} and R^{96} , R^{99} and R^{100} , or R^{107} and R^{108} are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)- NR^{201} -(C2-6 alkylene)-, wherein R^{201} is a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R^{101} , R^{103} and R^{105} are each independently (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl or (4) Cyc3, or C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc3;

Cyc3 has the same meaning as Cyc1, and Cyc3 may be substituted with 1-5 of R^{109} ;

R^{109} has the same meaning as R^{51} ;

R^3 and R^4 each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) $-\text{COOR}^{120}$, (6) $-\text{CONR}^{121}\text{R}^{122}$, (7) Cyc4 or (8) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) nitrile, (c) Cyc4, (d) $-\text{COOR}^{120}$, (e) $-\text{CONR}^{121}\text{R}^{122}$, (f) $-\text{OR}^{123}$, (g) $-\text{SR}^{124}$, (h) $-\text{NR}^{125}\text{R}^{126}$, (i) $-\text{NR}^{127}\text{COR}^{128}$, (j) $-\text{SO}_2\text{NR}^{129}\text{R}^{130}$, (k) $-\text{OCOR}^{131}$, (l) $-\text{NR}^{132}\text{SO}_2\text{R}^{133}$, (m) $-\text{NR}^{134}\text{COOR}^{135}$, (n) $-\text{NR}^{136}\text{CONR}^{137}\text{R}^{138}$, (o) $-\text{S-SR}^{139}$, (p) $-\text{NHC(=NH)NHR}^{140}$, (q) keto, (r) $-\text{NR}^{145}\text{CONR}^{146}\text{COR}^{147}$ and (s) $-\text{N(SO}_2\text{R}^{133})_2$;

$\text{R}^{120}-\text{R}^{130}$, R^{132} , R^{134} , $\text{R}^{136}-\text{R}^{138}$, R^{145} and R^{146} each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc4 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4, halogen, $-\text{OR}^{148}$, $-\text{SR}^{149}$, $-\text{COOR}^{150}$ or $-\text{NHCOR}^{141}$, or

R^{121} and R^{122} , R^{129} and R^{130} , or R^{137} and R^{138} are taken together to represent (1) C2-6 alkylene, (2) $-(\text{C2-6 alkylene})-\text{O}-(\text{C2-6 alkylene})-$, (3) $-(\text{C2-6 alkylene})-\text{S}-(\text{C2-6 alkylene})-$ or (4) $-(\text{C2-6 alkylene})-\text{NR}^{201}-(\text{C2-6 alkylene})-$, wherein R^{201} represents a hydrogen atom, C1-8 alkyl, phenyl, C1-8 alkyl substituted with phenyl;

R^{131} , R^{133} , R^{135} , R^{139} and R^{147} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc4 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4, halogen, $-\text{OR}^{148}$, $-\text{SR}^{149}$, $-\text{COOR}^{150}$ or $-\text{NHCOR}^{141}$;

R^{140} represents a hydrogen atom, $-\text{COOR}^{142}$ or $-\text{SO}_2\text{R}^{143}$;

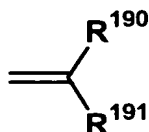
$\text{R}^{141}-\text{R}^{143}$ each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc4 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4;

$\text{R}^{148}-\text{R}^{150}$ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc4 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4;

Cyc4 has the same meaning as Cyc1, and Cyc4 may be substituted with 1-5 of R¹⁴⁴;

R¹⁴⁴ has the same meaning as R⁵¹, or

R³ and R⁴ are taken together to represent



wherein R¹⁹⁰ and R¹⁹¹ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) -COOR¹²⁰, (6) -CONR¹²¹R¹²², (7) Cyc4 or (8) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) nitrile, (c) Cyc4, (d) -COOR¹²⁰, (e) -CONR¹²¹R¹²², (f) -OR¹²³, (g) -SR¹²⁴, (h) -NR¹²⁵R¹²⁶, (i) -NR¹²⁷COR¹²⁸, (j) -SO₂NR¹²⁹R¹³⁰, (k) -OCOR¹³¹, (l) -NR¹³²SO₂R¹³³, (m) -NR¹³⁴COOR¹³⁵, (n) -NR¹³⁶CONR¹³⁷R¹³⁸, (o) -S-SR¹³⁹, (p) -NHC(=NH)NHR¹⁴⁰, (q) keto, (r) -NR¹⁴⁵CONR¹⁴⁶COR¹⁴⁷ and (s) -N(SO₂R¹³³)₂;

R¹²⁰-R¹⁴⁰ and R¹⁴⁵-R¹⁴⁷ have the same meanings as described above;

R⁵ represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) Cyc5 or (4) C1-8 alkyl substituted with Cyc5;

Cyc5 has the same meaning as Cyc1, and Cyc5 may be substituted with 1-5 of R¹⁵⁰;

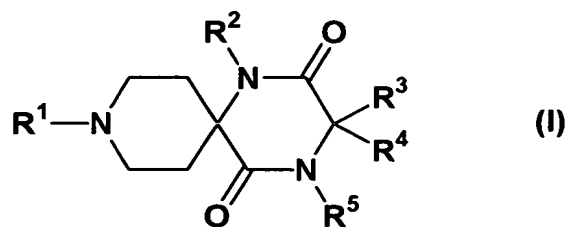
R¹⁵⁰ has the same meaning as R⁵¹;

an N-oxide thereof, a salt thereof, or a prodrug thereof.

11. A medicament which comprises a function inhibitor of an effector cell comprising a CCR5 antagonist, in combination with one, two or more immunosuppressive drug(s).

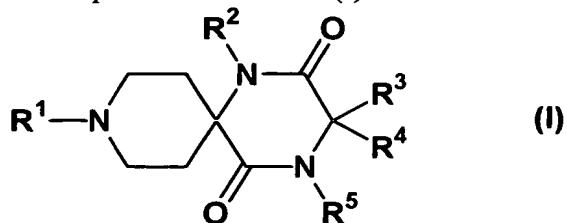
12. The medicament according to claim 11, wherein the one, two or more immunosuppressive drug(s) are selected from the group of tacrolimus, cyclosporine, sirolimus, corticosteroid, azathioprine, mycophenolate mofetil, FTY-720 and cyclophosphamide.

13. A method for prevention and/or treatment of a disease caused by effector cell function, which comprises administering to a mammal an effective amount of a compound of formula (I)



wherein all symbols have the same meanings as those defined in claim 10, an N-oxide thereof, a salt thereof, or a prodrug thereof.

14. Use of a compound of formula (I)



wherein all symbols have the same meanings as those defined in claim 10,

an N-oxide thereof, a salt thereof, or a prodrug thereof for the manufacture of an agent for prevention and/or treatment of a disease caused by effector cell function.